



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,158	05/23/2001	David J. Ecker	ISIS-4766	9473

32650 7590 02/03/2005

WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE - 46TH FLOOR
PHILADELPHIA, PA 19103

EXAMINER

SODERQUIST, ARLEN

ART UNIT	PAPER NUMBER
----------	--------------

1743

DATE MAILED: 02/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/863,158

Applicant(s)

ECKER ET AL.

Examiner

Arlen Soderquist

Art Unit

1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26-32, 34-40 and 42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26-32, 34-40 and 42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1743

1. The disclosure is objected to because of the following informalities: the current status of the continuity data needs to be updated and the title of the invention is not descriptive of the claimed invention.

Appropriate correction is required.

2. Claims 26-32, 34-40 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a porous reaction support and the first and second surfaces of the reaction support being substantially parallel, does not reasonably provide enablement for another means of transferring fluid from the first to the second surface or the first and second surfaces not being substantially parallel. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification fails to teach any other means of transporting to or making the fluids jetted on the first surface available for collection at the second surface. There also not anything that would teach one of skill in the art to have the second surface be a surface that is not substantially perpendicular with the first surface. Additionally, relative to claim 38 and the claims dependent therefrom, the specification, while being enabling for breaking the bond between the support and the reaction product, does not reasonably provide enablement for removal from the support by any other means.

3. Claims 26-32 and 34-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 26 does not provide structure or a method step that makes the reaction product available to collect from the second surface. In claim 32 it is not clear if there are multiple second surfaces of which one is substantially parallel to the first or if the claim is trying to further define the second surface. It appears that the changes omitted structure and/or method steps essential to the performance of the method. See MPEP § 2172.01.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1743

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. Claims 26-27, 29, 32, 34-40 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baldeschwieler (US 5,847,105) in view of the admitted state of the prior art, Koester (US 4,923,901) and Salmon. In the patent Baldeschwieler teaches method and apparatus for performing multiple sequential reactions on a matrix. In the method a substrate is prepared upon which microdrop-sized loci are located at which chemical compounds are synthesized or diagnostic tests are conducted. The loci are formed by applying microdrops from a dispenser from which a microdrop is pulse fed onto the surface of the substrate. Column 1 lines 14-25 teach that the apparatus and method are useful for performing a test or synthesis involving sequential steps such as DNA sequencing, DNA diagnostics, oligonucleotide and peptide synthesis, screening tests for target DNA, RNA or polypeptides, synthesis of diverse molecules, DNA separation technology whereby DNA binds to target molecules, preparation of polysaccharides, methods for making complementary oligonucleotides, and any other test, sequencing or synthetic method utilizing a sequence of steps at a locus. An advantage or improvement can be obtained by providing loci so that combinations of different reactions may be conducted on the same matrix. The summary of column 2 teaches how the synthesis steps are performed. In the case of delivery of reagents that become attached to the surface, the invention provides a substrate having a surface to which a first reagent can be attached by dispensing microdrops of the reagent in liquid form onto the substrate. The dispenser is displaced relative to the surface and at least one microdrop is applied thereto containing the same or a different reagent. By repeating this using the same or a different first reagent in liquid form, a plurality of loci on the surface may be prepared wherein the reagents covalently attach at microdrop-sized loci wherein the boundaries of each locus are not contiguous to any adjacent locus. The surface may then be washed to remove unattached reagent. If needed, the entire surface may be treated,

Art Unit: 1743

or alternatively, a selected subset of loci may be treated, with deprotecting reagents to expose reactive sites of the molecules attached to the surface. The deprotecting reagent may also be dispensed from the device. Then one or more microdrops containing a second reagent in liquid form may be dispensed at selected loci on the substrate surface, whereby the second reagent is selected to react with the molecules already attached to the matrix. The dispenser is again displaced relative to the surface to apply the second reagent at different loci using the same or a different second reagent which reacts with the respective attached molecules. Again, the entire surface will be washed to remove unreacted second reagents. Then the entire surface or selected subsets of loci may be treated with deprotecting agents, and this process may be repeated.

Column 3, lines 27-33 teach the substrate as a solid, such as glass, prepared to receive linkers attached to the surface. Porous substrates, such as paper or synthetic filters may be used, as well as filters having straight, parallel micropores (such as sold by Nucleopore). In such a microporous substrate, the reactions may take place within the pores, thus amplifying the potential signal at the locus. Column 6 lines 46-67 discuss the ink-jet used to dispense the microdroplets. Column 3, lines 4-14 of Baldeschwieler discuss the removal of the formed compounds either selectively or non-selectively for diagnostic assays or isolation of the final compound(s). Baldeschwieler does not teach using a collection plate to collect the synthesis products.

In the paper Salmon teaches discovery of biologically active peptides from a library synthesized on solid supports. Pages 11709 and figure 3 teach the two-stage release of the peptide from the support for testing purposes. In the method a plurality of beads is first added to wells (donor chambers) of a 96-well microassay filtration plate. A portion of the bound peptide is released from the support and transferred from the filtration plate to a corresponding assay plate (acceptor chambers) and reagent is added. The beads from wells that a reaction with the reagent occurred are then individually loaded into wells of a microassay filtration plate and the additional peptide is released, transferred to a corresponding assay plate and a reagent added. In the paragraph bridging pages 11711 and 11712 Salmon teaches fluid volumes for the wells can be in the range of 10 - 100 μ l.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a collection or assay plate into the methods of Baldeschwieler because

Art Unit: 1743

of the ability to carry out further tests on the synthesized materials or to isolate the individual compounds for analysis as taught by Salmon and Baldeschwieler.

6. Claims 28 and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baldeschwieler in view of Salmon as applied to claims 26-27, 29, 32, 34-40 and 42 above, and further in view of the admitted state of the prior art and/or Koester (US 4,923,901). Although Baldeschwieler teaches porous substrates, such as paper, synthetic filters and filters having straight, parallel micropores, the full scope of the materials are not taught.

Page 15, line 22 to page 16, line 3 of the instant specification teach that several of the possible support are either known or commercially available. Specifically, supports include CPG (controlled pore glass) available from various distributors including CPG Inc./Millipore Corp.; RAPP copolymer, a highly crosslinked polystyrene, sold as TentaGel or a like product HLP (high loaded polystyrene) sold by ABI Corp.; Primer Support, a highly crosslinked polystyrene, sold by Pharmacia; POROS-OS polystyrene sold by PerSeptive, MPG (a magnetic pore glass) sold by CPG Inc.; Nucleic Acid Membrane Support sold by Millipore. Other useful supports include membranes sold by the Amicon division of W. R. Grace, Inc., and those sold by Gelman Sciences. Other membrane supports include membranes as described or referenced in U.S. Pat. No. 4,923,901 (Koester) assigned to Millipore Corp.; various supports as described in patent application WO 94/05394 and references cited therein; and various supports as described in patent application WO 90/02749 including activated polystyrene layer on a polyethylene membrane (this list includes at least the synthetic filters of Baldeschwieler).

The Koester patent was cited in the instant specification as disclosing supports usable for the instant methods. More specifically Koester teaches a method for synthesizing oligonucleotides and peptides directly onto a membrane. The method provides a means for generating membrane affinity supports. A modified membrane for the method of direct synthesis is also provided. The introduction of the patent teaches various supports that are known to be used in solid phase peptide and oligonucleotide synthesis. These supports include beaded material such as cellulose, glass beads, Sephadex, Sepharose, agarose, polyacrylamide, porous particulate alumina, hydroxyalkyl methacrylate gels, diol-bonded silica or porous ceramics, flat material such as filter disc of nylon and nitrocellulose, glass beads of controlled porosity. A membrane, a being flat and highly porous, mechanical stable material, would be most

Art Unit: 1743

advantageous as affinity support, because it could be handled easily, cut into various sizes, stacked on top of each other for upscaling purposes and reused several times. Furthermore, the support should be chemically stable under the conditions of oligonucleotide and peptide synthesis and should not show non-specific binding of either nucleic acids or proteins as this would give rise to a sensitivity-reducing background interaction. The membranes of Koester are taught as fulfilling these requirements or providing these advantages (this list also includes at least the synthetic filters of Baldeschwieler).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the admitted known synthesis supports or those of Koester into the methods of Baldeschwieler because of the known advantages of the porous supports as taught by Koester and the fact that the respective lists at least include the synthetic filters of Baldeschwieler and as shown by Koester the materials are known as supports for synthesis of oligonucleotides.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 26-32, 34-40 and 42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 5,925,732. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims totally encompass the patented claims and one could not practice the patented invention without infringing the instant claims.

9. Applicant's arguments filed December 9, 2004 have been fully considered but they are not persuasive. It is first pointed out that no terminal disclaimer has been filed although it was

Art Unit: 1743

indicated in the response that one was being filed with the response. Thus that rejection has not been overcome and is maintained. Examiner agrees that no reference of record anticipates the claims and has also withdrawn most of the art rejections. However the obviousness rejections based on Baldeschwieler have been appropriately modified. First regarding the statement that "the examiner must show reasons that the skilled artisan, confronted with the same problem as the inventor and with no knowledge of the claimed invention would select from the elements of the cited prior art for combination in the manner claimed". This is assuming that examiner has no more than the problem which applicant faced and the art that was before applicant at the time. This is not the standard for obviousness this is simply an allegation that examiner has used impermissible hindsight. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Applicant's representative questions the sufficiency of the obviousness rejection(s) under 35 U.S.C. § 103 in the context of lack of suggestion or adequate motivation to arrive at the claimed combination. No doubt that the "suggestion" or "adequate motivation" is required to combine references. See *In re Geiger*, 2 USPQ 2d 1276, 1278 (Fed. Cir. 1987). The suggestion or motivation, however, need not be specifically disclosed in references. See *In re Nilssen*, 7 USPQ 2d 1500 (Fed. Cir. 1988). The suggestion or motivation is defined not only in the context of the scope and content of the prior art references but also in the context of the level of one of ordinary skill in the art. *Graham v. John Deere Co.*, 148 USPQ 459 (Sup. Ct. 1963). That is, references are evaluated by what they suggest to one versed in the art rather than by their specific disclosure. See *In re Bozek*, 163 USPQ 545 (CCPA 1969); *In re Boe*, 148 USPQ 507 (CCPA 1966); *In re Preda*, 159 USPQ 342 (CCPA 1968); and *In re Shepard*, 138 USPQ 148 (CCPA 1963). The key to resolving the question of obviousness is therefore, dependent on the level of one skilled in the art. An artisan is presumed to have skill rather than a lack of skill. See *In re Sovish*, 226 USPQ 771 (Fed. Cir. 1985). The level of one skilled in the art, albeit not specifically defined due to its transient nature, encompasses at least engineering logic and

Art Unit: 1743

common sense logic applicable in the art in addition to those disclosed in the prior art references. Therefore standard for obviousness is does the applied art and/or the level of skill in the art present sufficient motivation to combine the teachings of the references to arrive at the claimed invention. In the instant case there is ample support of the combination. First Baldeschwieler is performing the type of synthesis as applicant is claiming in which the reactants are delivered to a porous support by the method which applicant is claiming. Additionally the type of support includes paper, synthetic filters and filters having straight, parallel micropores. The last one is particularly relevant to the limitations of claims 30 and 32 in which the transport is substantially normal to the surface. Finally, in column 3 lines 4-26, Baldeschwieler teaches removal of the synthesized compounds for analysis or testing. Applicant is right that Baldeschwieler does not teach using a collecting plate to collect the reaction after it has been released from the support. However the Salmon reference clearly teaches synthesis of compounds on a support followed by cleavage of the compounds for testing which is one of the purposes of Baldeschwieler. Thus the way Salmon does this is relevant to the instant claims. It is clear from Salmon that using the collection plate preserves the location identity of the compounds for further testing which would have been recognized as important to Baldeschwieler (at least one motivational reason). Relative to the rejection of Baldeschwieler in view of the admitted state of the art and/or Koester applicant is directed to *In re Leshin*, 125 USPQ 416 (CCPA 1960) dealing with the selection of a known material based on its suitability for the intended use is within the skill of a routineer in the art. In this reference combination there is at least some overlap between the materials used by Baldeschwieler and the materials admitted as commercially available or taught in the Koester reference in combination with the materials in the Koester reference being known for use in oligonucleotide synthesis as a support material. Thus one of skill in the art would have been directly led by the teachings of the references to use the known materials for their known purpose in addition to the fact that there is an overlap of materials between the references.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

Art Unit: 1743

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (571) 272-1265. The examiner's schedule is variable between the hours of about 6:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

A general phone number for the organization to which this application is assigned is (571) 272-1700. The fax phone number to file official papers for this application or proceeding is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, reading "Arlen Soderquist". The signature is fluid and cursive, with a large loop at the end.

February 1, 2005

ARLEN SODERQUIST
PRIMARY EXAMINER